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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS  4  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS  5  FEB 05   German (DE) application and patent publication number format
                   changes
 NEWS  6  MAR 03   MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03   FRANCEPAT now available on STN
 NEWS  9  MAR 29   Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29   WPIFV now available on STN
 NEWS 11  MAR 29   No connect hour charges in WPIFV until May 1, 2004
 NEWS 12  MAR 29   New monthly current-awareness alert (SDI) frequency in RAPRA

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 APRIL 2004
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FILE 'HOME' ENTERED AT 15:06:11 ON 17 APR 2004

=> file medline, uspatful, wpids, biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:06:35 ON 17 APR 2004

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=> s HER2
L1 5815 HER2

=> s l1 and antibody
L2 2990 L1 AND ANTIBODY

=> s l1 and specific antibody
L3 821 L1 AND SPECIFIC ANTIBODY

=> s antibody () binding
L4 24061 ANTIBODY (W) BINDING

=> s l1 and l4
L5 581 L1 AND L4

=> s albumin fusion protein
L6 54 ALBUMIN FUSION PROTEIN

=> s l6 and l5
L7 0 L6 AND L5

=> d l1 ti abs ibib 1-5

L1 ANSWER 1 OF 5815 MEDLINE on STN
TI **HER2** FISH in breast cancer.
ACCESSION NUMBER: 2004181584 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15064487
TITLE: **HER2** FISH in breast cancer.
AUTHOR: Bartlett John M S; Forsyth Amanda
CORPORATE SOURCE: Division of Cancer and Molecular Pathology, University Department of Surgery, Glasgow Royal Infirmary, Scotland, UK.
SOURCE: Methods in molecular medicine, (2004) 97 89-101. Journal code: 101123138. ISSN: 1543-1894.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040414
Last Updated on STN: 20040416

L1 ANSWER 2 OF 5815 MEDLINE on STN
TI Only grading has independent impact on breast cancer survival after adjustment for pathological response to preoperative chemotherapy.
AB Our objective was to determine pretreatment factors with an independent impact on survival after adjusting for response to preoperative chemotherapy and to describe parameters predictive for achieving a pathological complete remission (pCR) after preoperative chemotherapy containing an anthracycline. We performed univariate and multivariate analyses to describe the impact of the following pretreatment characteristics of 240 primary breast cancer patients who received preoperative chemotherapy containing an anthracycline at our institution on disease-free survival (DFS), distant disease-free survival (DDFS) and overall survival (OS): age, stage, clinical tumor size, clinical nodal status, grading, and expression of estrogen receptor, progesterone receptor, **Her2**/neu, Ki67, Bcl-2 and p53. Afterwards, the response to preoperative chemotherapy was added to the multivariate model in order to evaluate which pretreatment parameters retained their

prognostic impact. In addition, univariate analysis was performed to describe pretreatment variables predictive for achieving a pCR. With a median follow-up of 6.4 years (range 0-10.4), only grading retained its independent impact on DFS, DDFS and OS [hazard ratio (HR) 1.5, 1.7 and 2.9, respectively; p<0.05] after adjusting for the strongest independent prognostic factors pathological T category at surgery (HR 1.6, 1.8 and 1.7, respectively; p<0.001) and pathological N category at surgery (HR 2.3, 2.4 and 2.1, respectively; p<0.001). Predictive factors for the achievement of pCR (p<0.05) were age under 35 years, lower stage or smaller clinical tumor size and higher expression of Bcl-2 at diagnosis. We conclude that only grading retained its independent prognostic impact on DFS, DDFS and OS after adjusting for pathological response of breast tumor and axillary lymph node metastases to preoperative chemotherapy. According to our data, it could be hypothesized that young patients with early tumor stage and small primary tumors might profit most from preoperative chemotherapy.

ACCESSION NUMBER: 2004180587 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15075668
TITLE: Only grading has independent impact on breast cancer survival after adjustment for pathological response to preoperative chemotherapy.
AUTHOR: Schneeweiss Andreas; Katretchko Julia; Sinn Hans-Peter; Unnebrink Kristina; Rudlowski Christian; Geberth Matthias; Beldermann Frank; Bastert Gunther; Strittmatter Hans-Joachim
CORPORATE SOURCE: Department of Gynecology and Obstetrics, University of Heidelberg, Vossstrasse 9, 69115 Heidelberg, Germany.. andreas.schneeweiss@med.uni-heidelberg.de
SOURCE: Anti-cancer drugs, (2004 Feb) 15 (2) 127-35. Journal code: 9100823. ISSN: 0959-4973.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040413
Last Updated on STN: 20040415

L1 ANSWER 3 OF 5815 MEDLINE on STN
TI Medullary carcinoma, provocative now as then.
AB The recent observation that studies of BRCA1-associated tumors contain a high proportion of medullary carcinomas and ductal carcinomas with medullary features has re-introduced pathologists to an old diagnostic problem. The term "medullary carcinoma" dates to the 19th century, but the modern entity was introduced in 1949 by Moore and Foote, who described a carcinoma with a lymphoid infiltrate, a favorable prognosis, and low frequency of metastasis. Almost three decades later, Ridolfi et al proposed specific criteria for diagnosis, resulting in an entity with an even more favorable prognosis and a lower incidence. The reproducibility and clinical relevance of the diagnosis have been questioned recently, and new criteria have been proposed and compared. The tumors typically express cytokeratin 7, often vimentin and S100-protein, but not cytokeratin 20. The usual ones are positive for p53 and negative for estrogen receptor, **Her2**/neu, and bcl-2. Medullary carcinomas express e-cadherin and beta-catenin more often than ordinary high-grade ductal carcinomas, and the former have genetic differences from the latter. The lymphoid infiltrate of medullary carcinomas is related to beta-actin fragments exposed by apoptotic cells. The present review discusses historical and recent developments and emphasizes diagnostic criteria.

ACCESSION NUMBER: 2004179840 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15074561
TITLE: Medullary carcinoma, provocative now as then.
AUTHOR: Eichhorn John H
CORPORATE SOURCE: James Homer Wright Pathology Laboratories, Massachusetts

General Hospital and Harvard Medical School, 55 Fruit St, Boston, MA 02114, USA.. JEICHHORN@PARTNERS.ORG
SOURCE: Seminars in diagnostic pathology, (2004 Feb) 21 (1) 65-73. Journal code: 8502262. ISSN: 0740-2570.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040413
Last Updated on STN: 20040413

L1 ANSWER 4 OF 5815 MEDLINE on STN
TI **HER2**-targeted therapy reduces incidence and progression of midlife mammary tumors in female murine mammary tumor virus huHER2-transgenic mice.
AB PURPOSE: This study examined the effectiveness of early and prolonged mu4D5 (the murine form of trastuzumab/Herceptin) treatment in transgenic mice that overexpress human **HER2** (huHER2), under the murine mammary tumor virus promoter, as a model of huHER2-overexpressing breast cancer. EXPERIMENTAL DESIGN: Mice were randomly assigned to one of three treatment groups and received i.p. injections from 17 weeks of age until either 52 weeks of age or morbidity. Fourteen mice received 100 mg/kg mu4D5, 14 mice received 100 mg/kg antiherpes simplex virus glycoprotein D control antibody, and 11 mice received a diluent control. RESULTS: High levels of huHER2 expression were detectable in mammary glands of young virgin founder mice. Mammary adenocarcinomas were frequently found in female founders and progeny at an average age of 28 weeks, with some progressing to metastatic disease. The incidence of mammary tumors was significantly reduced, and tumor growth inhibition was observed in mice receiving mu4D5 compared with control mice. In addition, Harderian gland neoplasms, highly associated with overexpression of huHER2 in this transgenic line, were entirely absent in the mu4D5 treatment group, indicating down-regulation of huHER2 in vivo activity. CONCLUSIONS: Early intervention with mu4D5 was of benefit in our transgenic mice at high risk for developing huHER2-overexpressing breast cancer. This study suggests a potential benefit of early treatment with Herceptin in **HER2**-positive primary breast cancer.
ACCESSION NUMBER: 2004178467 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15073130
TITLE: **HER2**-targeted therapy reduces incidence and progression of midlife mammary tumors in female murine mammary tumor virus huHER2-transgenic mice.
AUTHOR: Finkle David; Quan Zhi Ricky; Asghari Vida; Kloss Jessica; Ghaboosi Nazli; Mai Elaine; Wong Wai Lee; Hollingshead Philip; Schwall Ralph; Koeppen Hartmut; Erickson Sharon
CORPORATE SOURCE: Department of Physiology, Genentech, Inc., South San Francisco, California 94080, USA.
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2004 Apr 1) 10 (7) 2499-511.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040410
Last Updated on STN: 20040415

L1 ANSWER 5 OF 5815 MEDLINE on STN
TI Pathology of ovarian cancers in BRCA1 and BRCA2 carriers.
AB PURPOSE: Germline mutations in the BRCA1 and BRCA2 genes confer increased susceptibility to ovarian cancer. There is evidence that tumors in carriers may exhibit a distinct distribution of pathological features, but previous studies on the pathology of such tumors have been small. Our aim

was to evaluate the morphologies and immunophenotypes in a large cohort of patients with familial ovarian cancer. EXPERIMENTAL DESIGN: We performed a systematic review of ovarian tumors from 178 BRCA1 mutation carriers, 29 BRCA2 mutation carriers, and 235 controls with a similar age distribution. Tumors were evaluated by four pathologists blinded to mutation status. Both morphological features and immunochemical staining for p53 and **HER2** were evaluated. RESULTS: Tumors in BRCA1 mutation carriers were more likely than tumors in age-matched controls to be invasive serous adenocarcinomas (odds ratio, 1.84; 95% confidence interval, 1.21-2.79) and unlikely to be borderline or mucinous tumors. Tumors in BRCA1 carriers were of higher grade ($P < 0.0001$), had a higher percentage solid component ($P = 0.001$), and were more likely to stain strongly for p53 ($P = 0.018$). The distribution of pathological features in BRCA2 carriers was similar to that in BRCA1 carriers. CONCLUSIONS: Use of pathological features can substantially improve the targeting of predictive genetic testing. Results also suggest that BRCA1 and BRCA2 tumors are relatively aggressive and may be expected to have poor prognosis, although this may be treatment dependent.

ACCESSION NUMBER: 2004178464 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15073127
TITLE: Pathology of ovarian cancers in BRCA1 and BRCA2 carriers.
AUTHOR: Lakhani Sunil R; Manek Sanjiv; Penault-Llorca Frederique; Flanagan Adrienne; Arnout Laurent; Merrett Samantha; McGuffog Lesley; Steele Dawn; Devilee Peter; Klijn Jan G M; Meijers-Heijboer Hanne; Radice Paolo; Pilotti Silvana; Nevanlinna Heli; Butzow Ralf; Sobol Hagay; Jacquemier Jocylyne; Lyonet Dominique Stoppa; Neuhausen Susan L; Weber Barbara; Wagner Teresa; Winqvist Robert; Bignon Yves-Jean; Monti Franco; Schmitt Fernando; Lenoir Gilbert; Seitz Susanne; Hamman Ute; Pharoah Paul; Lane Geoff; Ponder Bruce; Bishop D Timothy; Easton Douglas F
CORPORATE SOURCE: The Breakthrough Toby Robins Breast Cancer Research Centre, Institute of Cancer Research, London, United Kingdom.. Sunil.Lakhani@icr.ac.uk
CONTRACT NUMBER: CA74415 (NCI)
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2004 Apr 1) 10 (7) 2473-81.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040410
Last Updated on STN: 20040415

=> d his

(FILE 'HOME' ENTERED AT 15:06:11 ON 17 APR 2004)

FILE 'MEDLINE, USPATFULL, WPIDS, BIOSIS' ENTERED AT 15:06:35 ON 17 APR 2004

L1 5815 S HER2
L2 2990 S L1 AND ANTIBODY
L3 821 S L1 AND SPECIFIC ANTIBODY
L4 24061 S ANTIBODY () BINDING
L5 581 S L1 AND L4
L6 54 S ALBUMIN FUSION PROTEIN
L7 0 S L6 AND L5

=> d l5 ti abs ibib 1-5

L5 ANSWER 1 OF 581 MEDLINE on STN

TI Vesicular stomatitis virus expressing a chimeric Sindbis glycoprotein containing an Fc **antibody binding** domain targets to **Her2**/neu overexpressing breast cancer cells.

AB Vesicular stomatitis virus (VSV) is a candidate for development for cancer therapy. It is an oncolytic virus that is safe in humans. Recombinant virus can be made directly from plasmid components. We attempted to create a virus that targeted specifically to breast cancer cells. Nonreplicating and replicating pseudotype VSV were created whose only surface glycoprotein (gp) was a Sindbis gp, called Sindbis-ZZ, modified to severely reduce its native binding function and to contain the Fc-binding domain of Staphylococcus aureus protein A. When titered on **Her2** /neu overexpressing SKBR3 human breast cancer cells, pseudotype VSV coated with Sindbis-ZZ had <1% the titer of pseudotype VSV coated with wild-type Sindbis gp. Titer was increased 50-fold when the Sindbis-ZZ pseudotype was conjugated with 4D5, a mouse monoclonal antibody directed against the **Her2**/neu receptor. Titers of antibody-conjugated virus were increased 36-fold on a second human breast cancer cell line, MCF7/H2, which expressed lower concentrations of **Her2**/neu receptor on the cell surface. At multiple concentrations of antibody, titers on SKBR3 cells were significantly greater when the virus was incubated with Herceptin, an antibody with a human Fc, than with 4D5, a mouse antibody, reflecting the known higher affinity of the protein A Fc-binding domain for human Fc. Analysis of the protein composition of the pseudotype VSV found low expression of the modified Sindbis gp on the virus accounting, in part, for a viral titer that did not exceed 1.2 x 10(5)/ml. This work demonstrates the ability to easily create, directly from plasmid components, an oncolytic replicating VSV with a restricted host cell range.

ACCESSION NUMBER: 2003572748 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14644615
TITLE: Vesicular stomatitis virus expressing a chimeric Sindbis glycoprotein containing an Fc **antibody binding** domain targets to **Her2**/neu overexpressing breast cancer cells.
AUTHOR: Bergman Ira; Whitaker-Dowling Patricia; Gao Yanhua; Griffin Judith A; Watkins Simon C
CORPORATE SOURCE: Departments of Pediatric, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA..
ira.bergman@chp.edu
SOURCE: Virology, (2003 Nov 25) 316 (2) 337-47.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040107
Entered Medline: 20040106

L5 ANSWER 2 OF 581 MEDLINE on STN

TI Growth factors and their receptors: new targets for prostate cancer therapy.

AB Stimulation of the signal transduction pathway of the epidermal growth-factor receptor (EGFR) tyrosine kinase family of receptors in tumor cells enhances cellular proliferation, prevents apoptosis, and promotes tumor-cell mobility, adhesion, and invasion. Therapeutic approaches used to target the EGFR and its signal transduction cascade include (1) monoclonal antibodies (eg, cetuximab [IMC-C225]) directed against the extracellular binding domain of the receptor; and (2) trastuzumab, a monoclonal **antibody binding** to the **HER2** receptor; immunotoxin conjugates use an antibody directed against EGFR joined to a cell toxin. All are in clinical trials for a number of cancers, including prostate cancer. Antisense strategies are in

preclinical development. Low-molecular-weight inhibitors of the EGFR tyrosine kinase also in clinical development include OSI-774, PD182905, PKI-166, CI-1033, and ZD1839. ZD1839 has shown encouraging results in patients with prostate cancer in phase 1 trials. mn

ACCESSION NUMBER: 2001457322 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11502465
TITLE: Growth factors and their receptors: new targets for prostate cancer therapy.
AUTHOR: Barton J; Blackledge G; Wakeling A
CORPORATE SOURCE: AstraZeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, United Kingdom.
SOURCE: Urology, (2001 Aug) 58 (2 Suppl 1) 114-22. Ref: 63
Journal code: 0366151. ISSN: 1527-9995.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010815
Last Updated on STN: 20020420
Entered Medline: 20011025

L5 ANSWER 3 OF 581 MEDLINE on STN
TI Inhibition of tumor growth by poly(ethylene glycol) derivatives of anti-ErbB2 antibodies.
AB Poly(ethylene glycol) (PEG) modification of substances with antitumor activity was shown to enhance penetration into growing solid tumors and extend antitumor effects. Accordingly, PEG was introduced as a modifier to two types of monoclonal antibodies (N12 and L26) specific to the ErbB2 (**HER2**) oncoprotein. These antibodies suppress the growth of tumors overexpressing ErbB2 (e.g. N87 human tumor) and the effect of PEG on their antitumor activity was evaluated. Methoxy-PEG-maleimide conjugated to sulfhydryl groups at the hinge region of the antibodies impaired their **antibody binding** to N87 tumor cells and did not enhance the antitumor inhibitory activity in tumor-bearing mice. A branched N-hydroxysuccinimide-activated PEG (PEG2), conjugated through amino groups of the protein, was used for binding to the whole antibody (Ab) or to its monomeric Fab' fragment. When tested against N87 cells in vitro, the binding activity and antitumor cytotoxic effects of Ab-PEG2 were mostly preserved. PEG2 modification did not seem to alter the tumor-inhibitory activity of the antibodies in vivo and the same pattern of tumor development was observed during the first few weeks following administration. However, the stimulating effects of PEG were observed at later stages of tumor growth since tumor development was either slowed down or completely arrested. Furthermore, a second tumor implanted into the same mice during this later stage was significantly or completely inhibited, as compared to results in mice injected with the unmodified antibody. The Fab'-PEG2 monomeric derivative was also shown to be effective in inhibiting the growth of a second tumor. The extended and prolonged enhancing effect of PEG on the antitumor activity of antibodies or Fab' fragments directed against ErbB2 may be of importance in the treatment of ErbB2-overexpressing neoplasms.

ACCESSION NUMBER: 2000418702 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10941905
TITLE: Inhibition of tumor growth by poly(ethylene glycol) derivatives of anti-ErbB2 antibodies.
AUTHOR: Hurwitz E; Klapper L N; Wilchek M; Yarden Y; Sela M
CORPORATE SOURCE: Department of Immunology, Weizmann Institute of Science, Rehovot, Israel.
SOURCE: Cancer immunology, immunotherapy : CII, (2000 Jul) 49 (4-5) 226-34.
Journal code: 8605732. ISSN: 0340-7004.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000905

L5 ANSWER 4 OF 581 MEDLINE on STN
TI Fractionation and characterization of polyclonal antibodies using three progressively more chaotropic solvents.
AB In the previous paper we described the effect of several different solvents on the structure of antibodies and demonstrated that 0.1 M glycine, pH 2.9, 7 M urea, pH 4.0, and 6 M guanidine-HCl, pH 4.0, unfold the antibodies to different degrees. Antibodies can be refolded from all of these solvents by dialysis. Polyclonal antibodies (pAbs) are a mixture of antibodies which recognize and bind different epitopes on the same antigen, with the strength of the antigen-**antibody binding** varying with each subpopulation. When rabbit antisera to the extracellular domain of **Her2** receptor (sHer2), derived from Chinese hamster ovary cells, was applied to an antigen column, bound pAbs were recovered with a step-wise elution of 0.1 M glycine, pH 2.9 (44% of the total recovered pAb), 7 M urea, pH 4.0 (29%), and 6 M guanidine-HCl, pH 4.0 (27%), with baseline resolution between them. Fluorescence spectra of the pAbs confirmed that the 0. 1 M glycine pH 2.9 sample had near-native structure, the pAbs in 7 M urea, pH 4.0, were partially unfolded, and the pAbs in the 6 M guanidine-HCl, pH 4.0, were totally unfolded. The glycine- or urea-eluted sample was refolded by dialysis into PBS, while the guanidine-HCl-eluted sample was first dialyzed into the 7 M urea pH 4.0 buffer and then into PBS. The refolded material from glycine or urea had native-like spectra, while the spectrum of the protein refolded from 6 M guanidine-HCl was slightly perturbed. All three of these subpopulations of pAbs formed antigen-antibody complexes which could be isolated by gel-filtration chromatography, precipitated sHer2 during immunoprecipitation, and recognized sHer2 in Western blots. The guanidine-HCl-eluted material was most sensitive for Western blotting. Identical results were obtained with pAbs applied either in the batch mode or to the top of the column, indicating that antibody aggregation which may occur when applied from the top of the column is not responsible for the distribution of pAbs into different subpopulations. These results indicate that the sequential use of these three increasingly chaotropic solvents to elute antibodies results in both increased recovery of antibodies and fractionation of pAbs into subpopulations with potentially different antigen binding characteristics.

ACCESSION NUMBER: 1998035672 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9367510
TITLE: Fractionation and characterization of polyclonal antibodies using three progressively more chaotropic solvents.
AUTHOR: Narhi L O; Caughey D J; Horan T P; Kita Y; Chang D; Arakawa T
CORPORATE SOURCE: Amgen Inc., Amgen Center, Thousand Oaks, California, 91320-1789, USA.
SOURCE: Analytical biochemistry, (1997 Nov 15) 253 (2) 246-52. Journal code: 0370535. ISSN: 0003-2697.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 20000303
Entered Medline: 19971216

L5 ANSWER 5 OF 581 MEDLINE on STN

TI Bispecific **HER2** x CD3 antibodies enhance T-cell cytotoxicity in vitro and localize to **HER2**-overexpressing xenografts in nude mice.

AB Recently, we reported the development of fully humanized bispecific F(ab')2 antibodies with dual binding specificities to human T-lymphocytes and to tumor cells overexpressing **HER2**. These antibodies were shown to effectively mediate targeted **HER2**-overexpressing tumor cell killing by freshly isolated human T-cells. In this report we extend our studies to describe the interaction of the bispecific antibody with activated T-lymphocytes (ATL) maintained in culture for an extended period of time. A microtiter plate radioreceptor assay was used to elucidate the affinity of bispecific **antibody binding** to ATL. The data show that ATL maintained in vitro for up to 5 weeks continued to express high-affinity CD3 surface markers that bound to bispecific antibody with a Kd of 2.49 nM and exerted cytolytic activities against targets overexpressing **HER2**. In addition, we demonstrated the specific localization of **HER2** x CD3 bispecific antibody to **HER2**-overexpressing tumor xenografts in nude mice. Furthermore, **HER2** x CD3 bispecific antibody has the ability to inhibit the proliferative activities of breast tumor (SKBR-3) cells in vitro. The clinical implications of these data are discussed.

ACCESSION NUMBER: 95129296 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7828373
TITLE: Bispecific **HER2** x CD3 antibodies enhance T-cell cytotoxicity in vitro and localize to **HER2** -overexpressing xenografts in nude mice.
AUTHOR: Shalaby M R; Carter P; Maneval D; Giltinan D; Kotts C
CORPORATE SOURCE: Department of BioAnalytical Technology, Genentech, Inc., South San Francisco, California 94080-4990.
SOURCE: Clinical immunology and immunopathology, (1995 Feb) 74 (2) 185-92.
Journal code: 0356637. ISSN: 0090-1229.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950307
Last Updated on STN: 20000303
Entered Medline: 19950221